EXTRA
Cerebrovascular Diseases

Cerebrovasc Dis Extra 2017;7:130–139

DOI: 10.1159/000479483
Received: May 15, 2017
Accepted: July 6, 2017
Published online: October 3, 2017

Original Paper

Pharyngolaryngeal Sensory Deficits in Patients with Middle Cerebral Artery Infarction: Lateralization and Relation to Overall Dysphagia Severity

Thomas Marian[a] Jens Burchard Schröder[a] Paul Muhle[a] Inga Claus[a] Axel Riecker[b] Tobias Warnecke[a] Sonja Suntrup-Krueger[a] Rainer Dziewas[a]

[a]Department of Neurology, University Hospital Münster, Münster, Germany;
[b]Neurological/Neurosurgical Rehabilitation Clinic, RehaNova, Cologne, Germany

Keywords

Stroke · Post-stroke dysphagia · Pharyngolaryngeal sensory deficits · Lateralization · Dysphagia severity

Abstract

Background: Dysphagia is a frequent and dangerous complication of acute stroke. Apart from a well-timed oropharyngeal muscular contraction pattern, sensory feedback is of utmost importance for safe and efficient swallowing. In the present study, we therefore analyzed the relation between pharyngolaryngeal sensory deficits and post-stroke dysphagia (PSD) severity in a cohort of acute stroke patients with middle cerebral artery (MCA) infarction. ***Methods:*** Eighty-four first-ever MCA stroke patients (41 left, 43 right) were included in this trial. In all patients, fiberoptic endoscopic evaluation of swallowing (FEES) was performed according to a standardized protocol within 96 h after stroke onset. PSD was classified according to the 6-point fiberoptic endoscopic dysphagia severity scale. Pharyngolaryngeal sensation was semi-quantitatively evaluated by a FEES-based touch technique. ***Results:*** PSD severity was closely related to the pharyngolaryngeal sensory deficit. With regards to lateralization of the sensory deficit, there was a slight but significant preponderance of sensory loss contralateral to the side of stroke. Apart from that, right hemispheric stroke patients were found to present with a more severe PSD. ***Conclusions:*** This study provides evidence that an intact sensory feedback is of utmost importance to perform nonimpaired swallowing and highlights the key role of disturbed pharyngeal and laryngeal afferents in the pathophysiology of PSD.

Dr. med. Thomas Marian
Department of Neurology, University Hospital Münster
Albert-Schweitzer-Campus 1
DE–48149 Münster (Germany)
E-Mail thomas.marian@ukmuenster.de

Introduction

Dysphagia is an important complication of acute stroke. Abnormal lip closure, lingual incoordination, and delayed or absent triggering of the swallowing reflex may lead to a disturbance of both the oral and the pharyngeal stage of swallowing. Frequently encountered consequences are incomplete oral clearance, pharyngeal pooling, regurgitation, and aspiration [1–6]. In the acute stage of the illness, dysphagia is found in up to 80% of all stroke patients, depending on the timing of the assessment, the diagnostic methods used, and the case mix [7–10]. Dysphagia symptoms resolve in a number of patients within a week to a month; however, even after 6 months, 11–50% of all patients suffer from impaired deglutition [4, 7]. Post-stroke dysphagia (PSD) is associated with increased mortality and morbidity due to pneumonia, dehydration, and malnutrition. Apart from the deleterious consequences of the clinical course in the individual stroke patient, PSD and, in particular, post-stroke pneumonia are also associated with prolonged length of hospital stay and significantly increased health care expenditures [9, 11, 12].

Apart from a finely tuned oropharyngeal muscular contraction pattern involving more than 25 different muscles, intact deglutition is highly dependent on sensory feedback [13]. Thus, the afferent input from food or saliva is important in the initiation of swallowing [1–4]. In addition, characteristics of the bolus, such as volume or viscosity, lead to a modulation of the motion sequence of swallowing. A larger bolus, for example, induces an earlier hyolaryngeal elevation as well as an earlier opening of the upper esophageal sphincter compared to a smaller bolus [7, 14]. Finally, protective mechanisms, in particular, clearing swallowing dealing with pharyngeal residues as well as a reflexive cough, are critically dependent on an intact sensory feedback [15–18]. The key role of afferent sensory information is also highlighted by new and emerging treatment strategies in this clinical domain. Thus, capsaicin and other pharmaceutical agents enhancing sensory input have been shown to improve swallowing safety in patients with dysphagia [19–21]. On the same note, pharyngeal electrical stimulation is supposed to promote rehabilitation of neurogenic dysphagia – at least in part – by restoring peripheral sensory feedback [22, 23].

In spite of the undeniable importance of sensory afferents from laryngeal and pharyngeal regions for safe and efficient swallowing, this topic is not in the focus of attention in most studies dealing with PSD. These studies usually use the risk of penetration and/or aspiration as endpoint by adopting a bedside aspiration screening [2, 4, 7, 12, 18, 24, 25]. If an instrumental assessment is employed, the penetration-aspiration scale [26] serves as the endpoint in most cases [12, 18], or more global scales, such as the functional oral intake scale, are considered [12].

In the present study, we analyzed the relationship between impaired pharyngolaryngeal sensation and overall dysphagia severity in a cohort of acute unilateral supratentorial stroke patients. In addition, we investigated to which extent pharyngolaryngeal sensory deficits were lateralized in these patients.

Patients and Methods

Patients

Eighty-four first-ever middle cerebral artery (MCA) stroke patients admitted to the Stroke or Intensive Care Unit of the University Hospital Münster, Münster, Germany, during a 14 months' period in 2014/2015, in whom fiberoptic endoscopic evaluation of swallowing (FEES) was carried out and who met the additional inclusion criteria, were enrolled in this trial. Patients with preexisting dysphagia, other comorbidities causing dysphagia, or a

Cerebrovascular Diseases EXTRA

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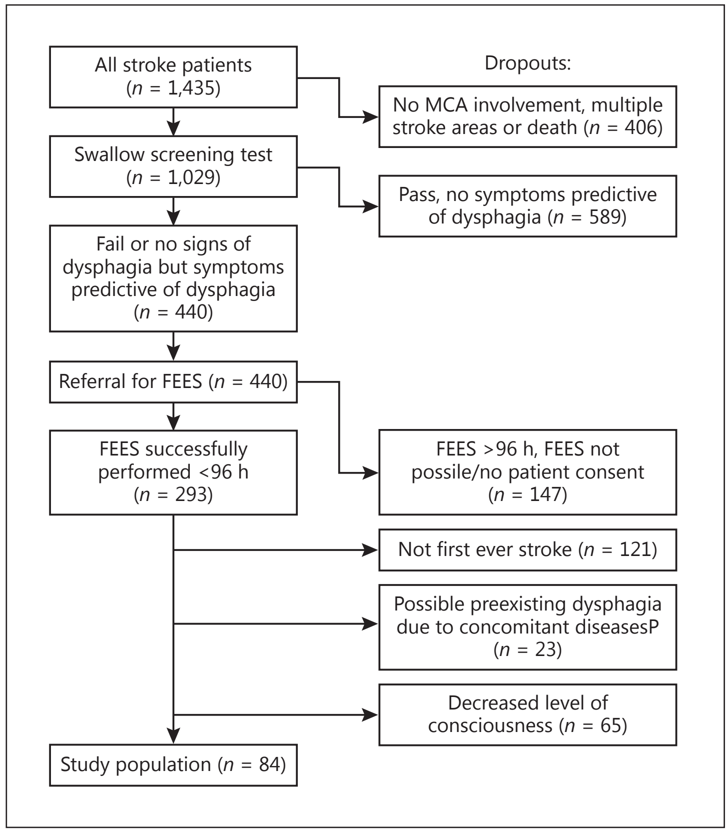

Fig. 1. Patient recruitment flow diagram detailing the number of evaluated and excluded patients.

decreased level of consciousness (NIH subcategory "Level of consciousness" >1) were excluded (Fig. 1). All examinations were part of our local routine diagnostic workup. Informed consent was obtained from all patients or their next of kin if the patients' communication was impaired. The study was approved by the local Ethics Committee.

Fiberoptic Endoscopic Evaluation of Swallowing

Following our in-house guidelines for stroke management, every patient who failed a simple water swallow screening test [27] or showed symptoms predictive for dysphagia, i.e., severe neurological deficit (NIHSS > 10 points), severe dysarthria/aphasia, or facial palsy [28] was further assessed with FEES within 96 h after stroke onset. The endoscopic evaluation was performed in accordance with our protocol for dysphagia assessment in acute stroke, which has been previously developed and validated [29, 30]. The equipment consisted of a flexible fiberoptic rhinolaryngoscope 3.1 mm in diameter (11101 RP2, Karl Storz, Tuttlingen, Germany), a light source and camera (rp Cam-X, rpSzene®, Rehder/Partner, Hamburg, Germany), a color monitor (WMP-226, Wincomm, Hsinchu, Taiwan), and a video camera (AUCC2WV3F, Computar, CBC group, Tokyo, Japan). All patients were examined by a neurologist together with a speech-language pathologist.

Measurement of Dysphagia Severity

Following our protocol [29], PSD was classified according to the 6-point fiberoptic endoscopic dysphagia severity scale (FEDSS) with a score of 1 being best and a score of 6 being worst, which has been described in detail elsewhere [30]. In brief, in case saliva pooling with penetration or aspiration was found, severe dysphagia was suspected and a score of 6 was assigned. Patients who were able to handle their saliva without penetration or aspiration next received a teaspoon full of mashed food. Those who showed penetration or aspiration without protective reflex (i.e., coughing or swallowing) in at least 1 of 3 attempts were again diagnosed with severe dysphagia (a FEDSS score of 5). If sufficient protective reflexes were present, this equaled to a FEDSS score of 4. Patients managing to eat mashed food without any penetration/aspiration events were exposed to a teaspoon of colored water. If penetration or aspiration was detected without sufficient protective reflex, the patient assigned a FEDSS score of 4, while the presence of protective reflexes led to a FEDSS score of 3. If patients were able to swallow liquids 3 times without penetration or aspiration, a small piece of white bread was given to them as a last test. Here, penetration or aspiration or massive residues (>50% of bolus size) in the valleculae or piriformis were taken as evidence of severe difficulty with the consistency of this food, resulting in a FEDSS score of 2. If none of these findings were observed in 3 consecutive trials, a FEDSS score of 1 was achieved.

Rating of Sensory Deficit

For evaluating pharyngolaryngeal sensory deficits, we used a simple FEES-based sensory test that was modified from previous studies [31, 32]. The pharyngeal sidewalls, the pharyngeal posterior walls, and the arytenoids were touched bilaterally with the tip of the endoscope. Pharyngolaryngeal sensation was classified on a 3-point scale as intact (in 0 patients) (immediate swallow, cough, or laryngeal adductor reflex), absent (in 2 patients) (no reaction at all), or reduced (in 82 patients) (any weak response). Prior to the start of the study, 2 raters were trained using 10 video samples. Both raters independently evaluated pharyngolaryngeal sensory deficits. In the case of disagreement between the raters, the findings were discussed until a consensus was reached. In general, interobserver reliability was excellent (kappa coefficient = 0.92). Each single rating was added up to generate a sum score for each patient. This sum score was calculated separately for both sides, ranging from 0 (best) to 6 (worst). Apart from that, a total sum score was calculated by adding up the ratings for the left and right side. This total score ranged from 0 (best) to 12 (worst).

Statistical Analysis

Statistical analyses were carried out using IBM SPSS 24 software (release 24.0). Patient characteristics are given as arithmetic mean and standard deviation (SD) for continuous variables and as frequency and percentage for categorical variables. For analyses of parametric continuous data, the t test was used. The χ^2 test was used to compare the proportions of subjects. For direct correlation, the Spearman correlation coefficient (r) was used.

Results

During the study period, 1,435 acute stroke patients were treated in our Stroke or Intensive Care Unit. Of these, 84 subjects fulfilled all inclusion criteria of this study (Fig. 1). The main epidemiological and clinical characteristics are summarized in Table 1. The mean age of all patients was 69.3 (± 15.6) years. 94% of the patients suffered from ischemic stroke and 6% from hemorrhagic stroke. 41 patients had a stroke in the left hemisphere, and 43 had a stroke in the right hemisphere. The patients had a mean NIHSS score on the admission of 16.3 (± 8.3). All subjects had PSD rated with the FEDSS. The mean dysphagia severity score was 3.6 (± 1.6). 22 patients (26.2%) had mild PSD (mean age 64.5 ± 9.1 years, NIHSS score 16.1 ± 8.0) characterized by a FEDSS score of 1 or 2, 32 (38.1%) had moderate PSD marked by a FEDSS score of 3 or 4 (mean age 71.8 ± 12.9 years, NIHSS score 16.3 ± 8.9), and in 30 (35.7%) patients (mean age 69.8 ± 11.6 years, NIHSS score 16.1 ± 8.1) severe dysphagia was

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Table 1. Patient characteristics

	MCA stroke			*p* value
	total (*n* = 84)	left (*n* = 41)	right (*n* = 43)	
Female gender, *n* (%)	43 (51.2)	24 (58.5)	19 (44.2)	0.28
Mean age ± SD, years	69±15.6	70±14.4	68.6±14.4	0.16
Ischemic stroke, *n* (%)	79 (94)	39 (95.1)	40 (93)	0.87
Hemorrhagic stroke, *n* (%)	5 (6)	2 (4.9)	3 (7)	0.53
Mean NIHSS score ± SD (on admission)	16.3±8.3	15.3±8.4	17.3±8.4	0.91
Thrombolyses applied, *n* (%)	40 (47.6)	19 (46.3)	21 (48.8)	0.65
Ischemic stroke etiology, *n* (%)				
Large-artery atherosclerosis	23 (27.4)	12 (29.3)	11 (25.6)	0.77
Cardioembolism	33 (39.3)	15 (36.6)	18 (41.9)	0.46
Small-vessel occlusion	0	0	0	1
Other determined etiology	7 (8.3)	3 (7.3)	4 (9.3)	0.59
Unknown etiology	16 (19)	8 (19.5)	8 (18.6)	1
Vascular risk factors, *n* (%)				
Hypertension	71 (84.5)	32 (78)	39 (90.7)	0.24
Hyperlipidemia	55 (65.5)	28 (68.3)	27 (62.8)	0.85
Diabetes mellitus	21 (25)	12 (29.3)	9 (20.9)	0.35
Smoking	18 (21.4)	9 (22)	9 (20.9)	1
Atrial fibrillation	40 (47.6)	23 (56.1)	17 (39.5)	0.18

MCA, middle cerebral artery; SD, standard deviation; NIHSS, National Institutes of Health Stroke Scale.

diagnosed – represented by a FEDSS score of 5 or 6. Penetration or aspiration of at least one type of food during the FEES was seen in 71 patients (84.5%). Overall, a close correlation between PSD severity and the pharyngolaryngeal sensory deficit (Spearman $r = 0.452$, $p < 0.01$) was found (Fig. 2). With regards to lateralization of the pharyngolaryngeal sensory deficit, we found that in both right and left hemispheric stroke patients the sensory deficit was more pronounced contralateral to the side of stroke (Fig. 3). Apart from that, right hemispheric stroke patients were found to present with a more severe PSD (MCA left: mean FEDSS score 3.3 ± 1.7; MCA right: mean FEDSS score 4 ± 1.4; *t* test, $p = 0.034$).

Discussion

In this study, we analyzed the relationship between impaired pharyngolaryngeal sensation and severity of PSD in a cohort of patients with acute stroke in the right or left MCA territory. We also studied the degree of lateralization of impaired pharyngolaryngeal sensation in the same patient group. The first main finding was that PSD was closely correlated with the extent of the pharyngolaryngeal sensory deficit. This result highlights the importance of an intact sensory feedback for the execution of safe and efficient swallowing, depicts disturbed pharyngeal and laryngeal afferents as a key issue in the pathophysiology of PSD, and corroborates findings from previous studies.

In the first study devoted to this topic, Kidd et al. [24] back in 1995 used a simple transoral touch technique directed towards the left and right pharyngeal wall to determine pharyngeal sensory deficits. Already in that study, a strong association between impaired pharyngeal sensation and video-fluoroscopically proven aspiration was shown [24]. A second study employed more refined sensory testing using electrical stimulation of the faucial pillars

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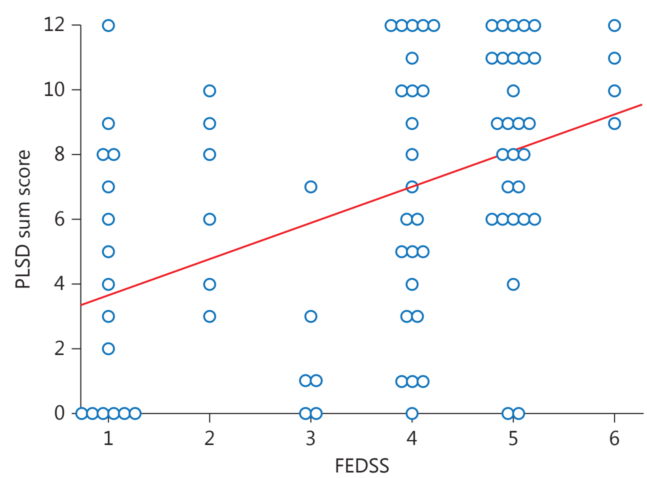

Fig. 2. Correlation of pharyngolaryngeal sensory deficits (PLSD) with post-stroke dysphagia severity (FEDSS, fiberoptic endoscopic dysphagia severity scale). The more pronounced the PLSD, the more distinct the post-stroke dysphagia severity (Spearman $r = 0.452$, $p < 0.01$).

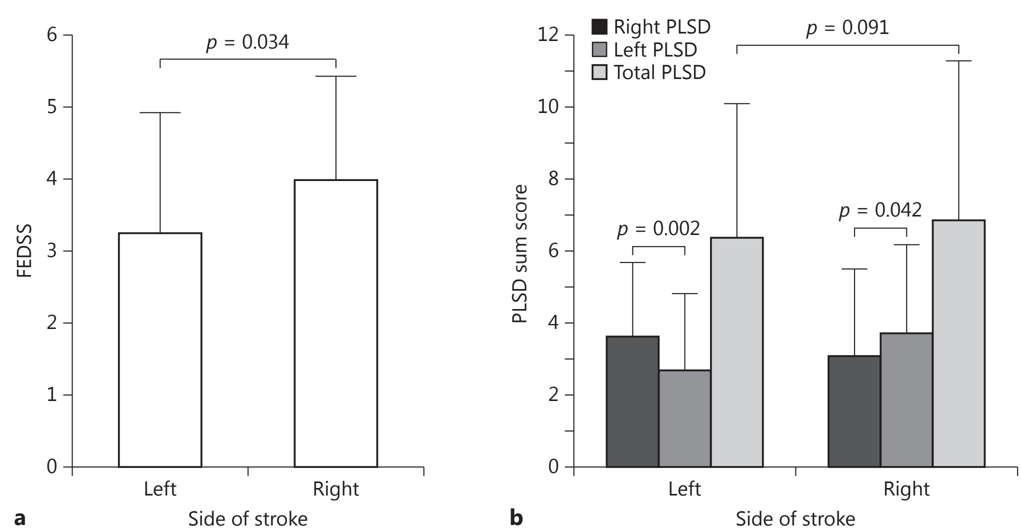

Fig. 3. a The mean fiberoptic endoscopic dysphagia severity scale (FEDSS) of the left and the right middle cerebral artery (MCA) are displayed. Patient with right MCA infarction present a more severe post-stroke dysphagia. *p* value is significant. **b** Lateralization of pharyngolaryngeal sensory deficits (PLSD) with regard to the affected side of stroke. The mean PLSD sum score of the left and the right MCA are displayed. The pharyngolaryngeal sensation was reduced bilaterally, although there was a significant pronunciation contralateral to the side of stroke. All *p* values are significant.

[17]. In that study, the degree of pharyngolaryngeal sensory deficit was also related to videofluoroscopically proven aspiration. In 2 further studies, Aviv et al. [15, 16] used FEES with laryngeal sensory testing recruiting 15 and 18 subacute stroke patients, respectively. Their main finding was that both in patients with clinically overt dysphagia and in patients without clinical signs of swallowing problems pharyngolaryngeal sensory deficits were highly prev-

alent and linked to aspiration. Finally, Onofri et al. [18] recruited 91 chronic stroke patients and used FEES for instrumental testing. Penetration and aspiration were chosen as dysphagia-related outcomes. Pharyngolaryngeal sensation was tested by touching the arytenoids and aryepiglottic folds with the tip of the endoscope. The investigators observed the highest incidence of either penetration or aspiration in patients with bilateral pharyngolaryngeal sensory loss.

The present study expands on these findings by recruiting acute stroke patients, a population group which is principally known to be at the highest risk of infectious airway complications [12, 33–36]. In addition, by using a multilevel rating of both dysphagia severity and pharyngolaryngeal sensory deficits, the association between both parameters could be highlighted very precisely for the first time. Interestingly, also under other medical conditions impaired pharyngolaryngeal afferents have been identified as a predictor of infectious complications. Thus, in the context of critical care medicine, dysphagia after extubating, the most important driver of extubating failure, has been shown to be mainly caused by pharyngolaryngeal sensory deficits [37–42]. In addition, in patients with chronic obstructive pulmonary disease, the swallow reflex is frequently delayed, predisposing those patients to aspiration and consecutively to exacerbations of their chronic pulmonary condition. Most likely, gastropharyngeal reflux with damage to the pharyngeal mucosa and resultant impaired sensory feedback constitutes the underlying pathophysiological link [43].

From a methodological point of view, the endoscopic approaches employed for sensory testing in the different studies need to be scrutinized. Thus, as stated above, Aviv et al. [15, 16] used pressure- and duration-controlled air pulses generated by an air-pulse stimulator and recorded the pressure that was necessary to elicit a laryngeal adductor reflex. In contrast to this, the study by Onofri et al. [18] as well as the present investigation used an equipment-wise less demanding touch technique, where different pharyngeal and/or laryngeal structures are touched with the tip of the flexible laryngoscope. Objective signs that sensory feedback is intact are reflexive coughing, gagging, throat clearing, or swallowing. Recently, Kaneoka et al. [44] compared both methods directly in a mixed patient group. They described that whereas impaired pharyngolaryngeal sensation as detected by the air-pulse method was not associated with penetration during the swallowing assessment, pharyngolaryngeal sensory loss revealed by the touch method was significantly correlated with an increased penetration-aspiration score. This result suggests that the touch method provides more clinically relevant results than the air-pulse method, and it was, therefore, chosen to determine pharyngolaryngeal sensation levels in the present investigation. In conjunction with the present investigation, it might therefore be concluded that the touch technique is a reliable method that should become a routine part of the FEES procedure at least in patients with suspected impaired sensory afferents.

As a second main result of our study, we found that pharyngolaryngeal sensation was reduced bilaterally in the examined regions, although there was a slight preponderance to the side contralateral to the stroke. This finding is in agreement with studies devoted to the central processing of pharyngolaryngeal sensory information. Thus, Teismann et al. [45], Lowell et al. [46], and Sörös et al. [47] showed that after unilateral oropharyngeal air-pulse stimulation primary and secondary sensory areas were activated bilaterally. Our results are also in keeping with a large body of animal studies providing convincing evidence that midline structures of the body, including the trunk, the perioral face, and the oral cavity, are not only represented contralateral but also in the ipsilateral primary sensory cortex [47, 48].

From a clinical point of view, the impact of a bilateral pharyngolaryngeal sensory impairment has also been highlighted by Onofri et al. [18]. In their study of chronic stroke patients, the risk of penetration or aspiration of any type of food more than doubled in patients featuring this condition as opposed to unilateral hypesthesia patients [18]. Finally, in our study group, patients with infarction in the territory of the right MCA had more severe PSD than patients with left-sided MCA strokes. This finding is in keeping with a recent imaging-based study showing that postcentral lesions, confined in particular to the right hemisphere, increase the risk of PSD [49, 50]. In addition this result also corroborates older studies suggesting that pharyngeal dysphagia is more frequent after right-sided strokes [1, 51].

There are some limitations of our study that need to be addressed. First, since we focused on strokes in the territory of the MCA for methodological reasons, our results and conclusions should not be generalized, without prior confirmation, to patients with other stroke localizations, in particular, patients with brainstem strokes. Second, although all patients received appropriate brain imaging, MRI was only performed in 57%. Therefore, we cannot rule out that a small proportion of patients included in this study had clinically silent lesions in the contralateral hemisphere or within the brainstem. Third, given the so-far unexplored impact of impaired pharyngolaryngeal sensory feedback on the cortical organization of swallowing in acute stroke, it would have been useful to add functional brain imaging, at least in some patients, to the experimental setup.

In conclusion, this study provides evidence for the importance of intact sensory feedback for the execution of safe and efficient swallowing and depicts disturbed pharyngeal and laryngeal afferents as a key issue in the pathophysiology of PSD.

Acknowledgements

The study was supported by the German Research Foundation (DFG SU 922/1-1, WO1425/6-1, and DZ 78/1-1).

Disclosure Statement

Thomas Marian, Jens Schröder, Inga Claus, and Axel Rieker declare no conflicts of interest. Paul Muhle received lecture fees from Olympus. Sonja Suntrup-Krueger received lecture fees from Abbvie, Fresenius Kabi, Nestle, and Boehringer Ingelheim. Tobias Warnecke received lecture fees from Abbvie, Teva, Bayer, and UCB, worked as a consultant for Abbvie and UCB, and received a research grant from Deutsche Parkinson Vereinigung e.V. (dPV). Rainer Dziewas received lecture fees from Nutricia, Fresenius Kabi, Boehringer Ingelheim, Bayer, Pfizer, Daiichi Sankyo, worked as a Consultant for Nestle, Daichii Sankyo, and InfectoPharm, and is member of the clinical advisory board of Phagenesis.

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